WEST Search History

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	L19	117 and 118	32
	L18	(113 or 115).ti,ab,clm.	13260
, and	L17	L16 same 115	140
П	L16	113 same 114	2349
, 12 2000-y-12	L15	GPP or GPDH or G3PP\$ or G3PDH or dehydrogenase or phosphatase	36159
	L14	transform\$	337857
	L13	glycerol	93423
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Tomai.	L12	13 and L11 not 15	0
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	L10	13 and L9 not 15	0
	L9	GPDH	20
	L8	G3PP\$	0
	L7	13 and L6 not 15	0
	L6	G3PDH	15
	L5	13 and L4	29
	L4	dehydrogenase or phosphatase	9635
	L3	11 and L2	241
	L2	transform\$	314651
	L1	glycerol	27437

END OF SEARCH HISTORY

Glycerol is an industrially useful material. However, other compounds may be derived from the glycerol biosynthetic pathway that also have commercial significance. For example, glycerol-producing organisms may be engineered to produce 1,3-propanediol (U.S. 5686276), a monomer having potential utility in the production of polyester fibers and the manufacture of polyurethanes and cyclic compounds. It is known for example that in some organisms, glycerol is converted to 3-hydroxypropionaldehyde and then to 1,3-propanediol through the actions of a dehydratase enzyme and an oxidoreductase enzyme, respectively. Bacterial strains able to produce 1.3-propanediol have been found, for example, in the groups Citrobacter, 10 Clostridium, Enterobacter, Ilyobacter, Klebsiella, Lactobacillus, and Pelobacter. Glycerol dehydratase and diol dehydratase systems are described by Seyfried et al. (1996) J. Bacteriol. 178:5793-5796 and Tobimatsu et al. (1995) J. Biol. Chem. 270:7142-7148, respectively. Recombinant organisms. 15 containing exogenous dehydratase enzyme, that are able to produce 1,3-propanediol have been described (U.S. 5686276). Although these organisms produce 1,3-propanediol, it is clear that they would benefit from a system that would minimize glycerol conversion.

There are a number of advantages in engineering a glycerol-producing 20 organism for the production of 1,3-propanediol where conversion of glycerol is minimized. A microorganism capable of efficiently producing glycerol under physiological conditions is industrially desirable, especially when the glycerol itself will be used as a substrate in vivo as part of a more complex catabolic or biosynthetic pathway that could be perturbed by osmotic stress or the addition of steering agents (e.g., the production of 1,3-propanediol). Some attempts at 25 creating glycerol kinase and glycerol dehydrogenase mutants have been made. For example, De Koning et al. (1990) Appl. Microbiol Biotechnol. 32:693-698 report the methanol-dependent production of dihydroxyacetone and glycerol by mutants of the methylotrophic yeast Hansenula polymorpha blocked in 30 dihydroxyacetone kinase and glycerol kinase. Methanol and an additional substrate, required to replenish the xyulose-5-phosphate co-substrate of the assimilation reaction, were used to produce glycerol; however, a dihydroxyacetone reductase (glycerol dehydrogenase) is also required. Similarly, Shaw and Cameron, Book of Abstracts, 211th ACS National Meeting. 35 New Orleans, LA, March 24-28 (1996), BIOT-154 Publisher: American Chemical Society, Washington, D. C., investigate the deletion of of ldhA (lactate dehydrogenase), glpK (glycerol kinase), and tpiA (triosephosphate isomerase) for the optimization of 1,3-propanediol production. They do not suggest the expression of cloned genes for G3PDH or G3P phosphatase for the



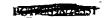
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protein having a glycerol-3-phosphatase activity. In addition to the G3PDH and G3P phosphatase genes, the host cell will contain disruptions in one or both of a gene encoding an endogenous glycerol kinase and a gene encoding an endogenous glycerol dehydrogenase. Where the production cell is designed to produce 1,3-propanediol, it will additionally contain a gene encoding a protein having a dehydratase activity.

The terms "foreign gene", "foreign DNA", "heterologous gene", and "heterologous DNA" all refer to genetic material native to one organism that has been placed within a different host organism.

The term "endogenous" as used herein with reference to genes or polypeptides expressed by genes, refers to genes or polypeptides that are native to a production cell and are not derived from another organism. Thus an "endogenous glycerol kinase" and an "endogenous glycerol dehydrogenase" are terms referring to polypeptides encoded by genes native to the production cell.

The terms "recombinant organism" and "transformed host" refer to any organism transformed with heterologous or foreign genes. The recombinant organisms of the present invention express foreign genes encoding G3PDH and G3P phosphatase for the production of glycerol from suitable carbon substrates. Additionally, the terms "recombinant organism" and "transformed host" refer to any organism transformed with endogenous (or homologous) genes so as to increase the copy number of the genes.

"Gene" refers to a nucleic acid fragment that expresses a specific protein, including regulatory sequences preceding (5' non-coding) and following (3' non-coding) the coding region. The terms "native" and "wild-type" gene refer to the gene as found in nature with its own regulatory sequences.

The terms "encoding" and "coding" refer to the process by which a gene, through the mechanisms of transcription and translation, produces an amino acid sequence. The process of encoding a specific amino acid sequence is meant to include DNA sequences that may involve base changes that do not cause a change in the encoded amino acid, or which involve base changes which may alter one or more amino acids, but do not affect the functional properties of the protein encoded by the DNA sequence. Therefore, the invention encompasses more than the specific exemplary sequences. Modifications to the sequence, such as deletions, insertions, or substitutions in the sequence which produce silent changes that do not substantially affect the functional properties of the resulting protein molecule are also contemplated. For example, alterations in the gene sequence which reflect the degeneracy of the genetic code, or which result in the production of a chemically equivalent amino acid at a given site, are contemplated; thus, a codon for the amino acid alanine, a



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example, genes isolated from prokaryotes include GenBank accessions M34393, M20938, L06231, U12567, L45246, L45323, L45324, L45325, U32164, U32689, and U39682. Genes isolated from fungi include GenBank accessions U30625, U30876 and X56162; genes isolated from insects include GenBank accessions X61223 and X14179; and genes isolated from mammalian sources include GenBank accessions U12424, M25558 and X78593.

Genes encoding G3P phosphatase are known. For example, GPP2 has been isolated from *Saccharomyces cerevisiae* and has the base sequence given by SEQ ID NO:5, which encodes the amino acid sequence given in SEQ ID NO:13 (Norbeck et al., (1996), *J. Biol. Chem.*, 271:13875).

For the purposes of the present invention, any gene encoding a G3P phosphatase activity is suitable for use in the method wherein that activity is capable of catalyzing the conversion of glycerol-3-phosphateand water to glycerol and inorganic phosphate. Further, any gene encoding the amino acid sequence of G3P phosphatase as given by SEQ ID NOS:13 and 14 corresponding to the genes GPP2 and GPP1 respectively, will be functional in the present invention including any amino acid sequence that encompasses amino acid substitutions, deletions or additions that do not alter the function of the G3P phosphatase enzyme. The skilled person will appreciate that genes encoding G3P phosphatase isolated from other sources will also be suitable for use in the present invention. For example, the dephosphorylation of glycerol-3-phosphate to yield glycerol may be achieved with one or more of the following general or specific phosphatases: alkaline phosphatase (EC 3.1.3.1) [GenBank M19159, M29663, U02550 or M33965]; acid phosphatase (EC 3.1.3.2) [GenBank U51210, U19789, U28658 or L20566]; glycerol-3-phosphatase (EC 3.1.3.-) [GenBank Z38060 or U18813x11]; glucose-1-phosphatase (EC 3.1.3.10) [GenBank M33807]; glucose-6-phosphatase (EC 3.1.3.9) [GenBank U00445]; fructose-1,6-bisphosphatase (EC 3.1.3.11) [GenBank X12545 or J03207] or phosphotidyl glycero phosphate phosphatase (EC 3.1.3.27) [GenBank M23546 and M23628].

Genes encoding glycerol kinase are known. For example, GUT1 encoding the glycerol kinase from *Saccharomyces* has been isolated and sequenced (Pavlik et al. (1993), *Curr. Genet.*, 24:21) and the base sequence is given by SEQ ID NO:6, which encodes the amino acid sequence given in SEQ ID NO:15. Alternatively, *glpK* encodes a glycerol kinase from *E. coli* and is characterized by the base sequence given in GeneBank L19201, base pairs 77347-78855.

Genes encoding glycerol dehydrogenase are known. For example, gldA encodes a glycerol dehydrogenase from E. coli and is characterized by the base

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buffer only. After the enzyme was added to the cuvette, an absorbance reading was taken. The first substrate, NADH (50 uL 4 mM NADH; absorbance should increase approx 1.25 AU), was added to determine the background rate. The rate should be followed for at least 3 min. The second substrate, DHAP (50 uL 40 mM DHAP), was then added and the absorbance change over time was monitored for at least 3 min to determine to determine the gross rate. G3PDH activity was defined by subtracting the background rate from the gross rate. 13C-NMR Assay for Glycerol Kinase Activity

An appropriate amount of enzyme, typically a cell-free crude extract, was added to a reaction mixture containing 40 mM ATP, 20 mM MgSO₄, 21 mM uniformly 13 C labelled glycerol (99%, Cambridge Isotope Laboratories), and 0.1 M Tris-HCl, pH 9 for 75 min at 25 °C. The conversion of glycerol to glycerol 3-phosphate was detected by 13 C-NMR (125 MHz): glycerol (63.11 ppm, d, J=41 Hz and 72.66 ppm, t, J=41 Hz); glycerol 3-phosphate (62.93 ppm, d, J=41 Hz; 65.31 ppm, br d, J=43 Hz; and 72.66 ppm, dt, J=6, 41 Hz).

NADH-linked Glycerol Dehydrogenase Assay

NADH -linked glycerol dehydrogenase activity in *E. coli* strains (*gldA*) was determined after protein separation by non-denaturing polyacrylamide gel electrophoresis. The conversion of glycerol plus NAD+ to dihydroxyacetone plus NADH was coupled with the conversion of 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) to a deeply colored formazan, using phenazine methosulfate (PMS) as mediator. (Tang et al. (1997) *J. Bacteriol*. 140:182).

Electrophoresis was performed in duplicate by standard procedures using native gels (8-16% TG, 1.5 mm, 15 lane gels from Novex, San Diego, CA). Residual glycerol was removed from the gels by washing 3x with 50 mM Tris or potassium carbonate buffer, pH 9 for 10 min. The duplicate gels were developed, with and without glycerol (approx. 0.16 M final concentration), in 15 mL of assay solution containing 50 mM Tris or potassium carbonate, pH 9, 60 mg ammonium sulfate, 75 mg NAD⁺, 1.5 mg MTT, and 0.5 mg PMS.

The presence or absence of NADH -linked glycerol dehydrogenase activity in *E. coli* strains (*gldA*) was also determined, following polyacrylamide gel electrophoresis, by reaction with polyclonal antibodies raised to purified *K. pneumoniae* glycerol dehydrogenase (*dhaD*).

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Items Description Set S1

'GLYCEROL 3-PHOSPHATE DEHYDROGENASE (NAD+)

GLYCEROLPHOSPHATASE RT Index-term

- **GLYCEROLPHOSPHATE**
- GLYCEROLPHOSPHATE ACYLTRANSFERASE *GLYCEROLPHOSPHATE DEHYDROGENASE
- 2 GLYCEROLPHOSPHATE DEHYDROGENASE
- GLYCEROLPHOSPHATE DEHYDROGENASE --ADMINISTRATI

- 457 GLYCEROLPHOSPHATE DEHYDROGENASE --ANTAGONISTS
 8 GLYCEROLPHOSPHATE DEHYDROGENASE --ANTAGONISTS
 9 144 GLYCEROLPHOSPHATE DEHYDROGENASE --BLOSYNTHESIS
 10 132 GLYCEROLPHOSPHATE DEHYDROGENASE --BLOOD --BL
 11 3 GLYCEROLPHOSPHATE DEHYDROGENASE --CEREBROSPINA
 12 GLYCEROLPHOSPHATE DEHYDROGENASE --CEREBROSPINA
 13 GLYCEROLPHOSPHATE DEHYDROGENASE --DEFICIENCY -13 GLYCEROLPHOSPHATE DEHYDROGENASE --DIAGNOSTIC U
 17 GLYCEROLPHOSPHATE DEHYDROGENASE --DIAGNOSTIC U
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 18 GLYCEROLPHOSPHATE DEHYDROGENASE --GRUGE EFFECTS

 - E13 E14 E16 E17 E18 E23 E23 E23
- 8 GLYCEROLPHOSPHATE DEHYDROGENASE --IMMUNOLOGY 110 GLYCEROLPHOSPHATE DEHYDROGENASE --ISOLATION AN
- 717 GLYCEROLPHOSPHATE DEHYDROGENASE -- METABOLISM
- **GLYCEROLPHOSPHATE DEHYDROGENASE --PHARMACOKINE**
- GLYCEROLPHOSPHATE DEHYDROGENASE --PHARMACOLOGY GLYCEROLPHOSPHATE DEHYDROGENASE --PHYSIOLOGY -
 - GLYCEROLPHOSPHATE DEHYDROGENASE --RADIATION EF GLYCEROLPHOSPHATE DEHYDROGENASE --URINE --UR

'GLYCEROLPHOSPHATE DEHYDROGENASE --GENETICS --G' 22

Ref Items Type RT Index-term

- 2 *GLYCEROLPHOSPHATE DEHYDROGENASE
- DC=D8.811.682.47.150.700.400. (GLYCEROLPHOSPHATE DEHYDROGENASE) 2906 X DC=D8.811.682.47.150.700.400. (GLYCER 1110 B 7 SUGAR ALCOHOL DEHYDROGENASES 222
- 2906 DC='D8.811.682.47.150.700.400.' (GLYCEROLPHOSPHATE DEHYDROGENASE)
- 102599 'RECOMBINANT PROTEINS' \$3 \$5 \$7 \$7 \$3 \$3
 - 68 S1 AND S3
- 100143 PHOSPHATASE 2 S5 AND S6 9 S2 AND S4 NOT S1
- 31066 GLYCEROL
- 123789 DEHYDROGENASE
 - 106 S9 AND S6 AND S10

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11/6/88 04348141 PMID: 61104

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Simplified, totally enzymatic method for determination of serum triglycerides with a centrifugal analyzer. Aug 1976

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Membrane permeability of hepatic mitochondria and lysosomes studied by structure-linked enzyme changes. Aug 1973

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Synthesis of 1-halo analogs of DL- glycerol 3-phosphate and their effects on glycerol phosphate dehydrogenase. Aug 4 1970

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The intramitochondrial distribution of some enzymes involved in the biosynthesis of rat-liver phospholipids. Feb 10 1970

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Regulation of the level of key enzymes of glycolysis and gluconeogenesis in liver. Sep 1969

11/6/104 02739879 PMID: 4309093

[Study of the enzymatic activities of liver and epididymal adipose tissue of Wistar H rats during a hyperlipidic diet. II. Reversibility when placed on the control diet] Etude des activities enzymatiques du foie et du tissu adipeux epididymaire du rat Wistar H au cours d'un regime hyperlipidique.

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Dietary response of various key enzymes related to glucose metabolism in normal and diabetic rat liver. Mar 22 1967

1/16/106 00032273 PMID: 14217903 THE CONTROL OF DISSIMILATION OF GLYCEROL AND L-ALPHA-GLYCEROPHOSPHATE IN ESCHERICHIA COLI. Sep 1964

09aug04 10:02:46 User208600 Session D1629.2

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Items Description 36001 GLYCEROL

128976 DEHYDROGENASE

105587 PHOSPHATASE

185 S1 AND S2 AND S3

231941 TRANSFORM?

5 S4 AND S5

73766 PLASMID 0 S7 AND S4

23 S9 AND S4 892502 GENE

6/6/1 0011502506 BIOSIS NO.: 199800296753
Differential expression of key enzymes of energy metabolism in preneoplastic and neoplastic rat liver lesions induced by N-nitrosomorpholine and

6/6/2 0011294579 BIOSIS NO.: 199800088826

Immortalization of human marrow stromal cells by retroviral transduction with a temperature sensitive oncogene: Identification of bipotential precursor cells capable of directed differentiation to either an osteoblast or adipocyte phenotype 1998

6/6/3 0010934031 BIOSIS NO.: 199799568091

Focal hepatic glycogenosis: A putative preneoplastic lesion associated with neoplasia and cirrhosis in explanted human livers 1997

6/6/4 0006748669 BIOSIS NO.: 198988063784 UNUSUAL HISTOCHEMICAL PATTERN IN PRENEOPLASTIC HEPATIC FOCI CHARACTERIZED BY HYPERACTIVITY OF SEVERAL

6/6/5 0004212934 BIOSIS NO.: 198477044845 ISOZYME PHENOTYPES OF POLYOMA VIRUS TUMORS IN MICE 1983

dentification of Ald6p as the target of a class of small-molecule suppressors of FK506 and their use in network dissection 2004 10/6/1 0014949973 BIOSIS NO.: 200400320730

10/6/2 0014921459 BIOSIS NO.: 200400292216

Expression of YAP4 in Saccharomyces cerevisiae under osmotic stress 200-

10/6/3 0014759536 BIOSIS NO.: 200400130293

Heterologous expression of Zygosaccharomyces rouxii glycerol 3-phosphate dehydrogenase gene (ZrGPD1) and glycerol dehydrogenase gene (ZrGCY1) in Saccharomyces cerevisiae. 2004

10/6/4 0014756741 BIOSIS NO.: 200400127498

Comparative metabolic flux analysis of lysine-producing Corynebacterium glutamicum cultured on glucose or fructose. 2004

Suppression of beta cell energy metabolism and insulin release by PGC-1alpha. 10/6/5 0014484056 BIOSIS NO.: 200300441090

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Regulation of D-arabitol and glycerol accumulation by Candida albicans in response to environmental stresses. 2003

Critical reduction in beta-cell mass results in two distinct outcomes over time. Adaptation with impaired glucose tolerance or decompensated diabetes. 2003 10/6/7 0014190057 BIOSIS NO.: 200300148776

Effects of benfluorex on fatty acid and glucose metabolism in isolated rat hepatocytes: From metabolic fluxes to gene expression 2002 10/6/8 0013869208 BIOSIS NO.: 200200462719

10/6/9 0013776639 BIOSIS NO.: 200200370150

Differential gene expression in brains of rats fed a ketogenic diet 2002

10/6/10 0013689700 BIOSIS NO.: 200200283211

Protein expression during lag phase and growth initiation in Saccharomyces cerevisiae 2002

10/6/11 0013290857 BIOSIS NO.: 200100462696

Time course of a 40 hour fast on pyruvate dehydrogenase activation and kinase expression in human skeletal muscle

10/6/12 0012899436 BIOSIS NO.: 200100071275

Molecular and physiological characterization of the NAD-dependent glycerol 3-phosphate dehydrogenase in the filamentous fungus Aspergillus nidulans 2001

10/6/13 0012883407 BIOSIS NO.: 200100055246

Microaerobic glycerol formation in Saccharomyces cerevisiae 2000

10/6/14 0012478366 BIOSIS NO.: 200000196679

Osteogenesis coordinated in C3H10T1/2 cells by adipogenesis-dependent BMP-2 expression system 2000

10/6/15 0011943915 BIOSIS NO.: 199900203575

Different signalling pathways contribute to the control of GPD1 gene expression by osmotic stress in Saccharomyces cerevisiae 1999

10/6/16 0011171712 BIOSIS NO.: 199799805772

Osmoresponsive proteins and functional assessment strategies in Saccharomyces cerevisiae 1997

10/6/17 0011063631 BIOSIS NO.: 199799697691

Modulation of glycerol and ethanol yields during alcoholic fermentation in Saccharomyces cerevisiae strains overexpressed or disrupted for GP encoding glycerol 3-phosphate dehydrogenase 1997

10/6/18 0010821522 BIOSIS NO:: 199799455582

1997 Osmoregulation and protein expression in a pbs2-DELTA mutant of Saccharomyces cerevisiae during adaptation to hypersaline stress

1996 Activation and regulation of the Spc1 stress-activated protein kinase in Schizosaccharomyces pombe 10/6/19 0010411623 BIOSIS NO.: 199699045683

10/6/20 0010138668 BIOSIS NO.: 19969860650

Evolution of beta-cell dysfunction in the male Zucker diabetic fatty rat 1995

10/6/21 0004593902 BIOSIS NO.: 198679012801 PROTEIN POLYMORPHISMS AND THEIR GENETIC CONTROL IN THE RED-BACKED VOLE CLETHRIONOMYS-RUFOCANUS-BEDFORDI

10/6/22 0003261624 BIOSIS NO.: 198171080583 ISOLATION AND PROPERTIES OF A BACILLUS-SUBTILIS MUTANT UNABLE TO PRODUCE FRUCTOSE BIS PHOSPHATASE EC-3.1.3.1 1981

106/23 0002353849 BIOSIS NO.: 197865014836 ISOLATION AND CHARACTERIZATION OF YEAST MUTANTS DEFECTIVE IN INTERMEDIARY CARBON METABOLISM AND IN CARBON CATABOLITE DE REPRESSION 1977

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Description GLYCEROL Items 57893

15009 DEHYDROGENASE

5001 S1 AND S2 AND S3 **PHOSPHATASE** 29088

141746 TRANSFORM? 4591 S4 AND S5

4347 S7 AND S4 42288 PLASMID

4788 S9 AND S4 78013 GENE

599 S1(S)S2(S)S3

544 S11 AND S5

14 S13 AND PY<1998 90 S11 (S)S5 \$14 \$15 \$15 \$17 \$18 \$18 \$19 \$20 \$21

493 S11 AND S8 493 S11(S)S8

60 S16 AND PY<1998 S17 NOT S14 4

572 S9 AND S11

S20 AND PY<1998 NOT (S18 OR S14) 357 S9 (S)S11

NOVEL METHODS OF DIAGNOSIS OF METASTATIC CANCER, COMPOSITIONS AND METHODS OF SCREENING FOR MODULATORS OF MATASTATIC CANCER NOUVEAUX PROCEDES DE DIAGNOSTIC D'UN CANCER METASTATIQUE, COMPOSITIONS ET PROCEDES DE DEPISTER DES MODULATEURS DU CANCER METASTATIQUE 13/TI/1 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

13/TI/2

13/TI/2 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. COMPUTER SYSTEMS AND METHODS FOR ASSOCIATING GENES WITH TRAITS USING CROSS SPECIES DATA SYSTEMES ET PROCEDES INFORMATIQUES PERMETTANT D'ASSOCIER DES GENES AVEC DES CARACTERISTIQUES AU MOYEN DE DONNEES HETEROSPECIFIQUES

1371/3 DIALOG(R)File 349;(c) 2004 WIPO/Univentio, All rts. reserv.
METHODS OF DETECTING SOFT TISSUE SARCOMA, COMPOSITIONS AND METHODS OF SCREENING FOR SOFT TISSUE SARCOMA MODULATORS PROCEDES DE DETECTION DU SARCOME DES TISSUS MOUS, COMPOSITIONS ET PROCEDES DE CRIBLAGE DES MODULATEURS DU SARCOME DES TISSUS MOUS.

13/TI/4 DIALOG(R)FIIe 349;(c) 2004 WIPO/Univentio All rts. reserv. STRUCTURE OF THE FARNESOID X RECEPTOR LIGAND BINDING DOMAIN AND METHODS OF USE THEREFOR STRUCTURE I DOMAINE DE FIXATION DU LIGAND DU RECEPTEUR FARNESOIDE X ET PROCEDES D'UTILISATION DE CELLE-CI

13/TI/5 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. NON-STEROIDAL FARNESOID X RECEPTOR MODULATORS AND METHODS FOR THE USE THEREOF MODULATEURS NON STEROIDIENS DU RECEPTEUR FARNESOIDE X ET METHODES

14/TI/1 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. resen. MORAXELLA CATARRHALIS OUTER MEMBRANE PROTEIN-106 POLYPEPTIDE, GENE SEQUENCE AND USES THEREOF POLYPEPTIDE DE LA PROTEINE-106 DE LA MEMBRANE EXTERNE DE MORAXELLA CATARRHALIS, SA SEQUENCE GENETIQUE ET SON UTILISATION

14/TI/2 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. NOVEL TYROSINE KINASE RECEPTORS AND LIGANDS NOUVEAUX RECEPTEURS DU TYPE TYROSINE KINASE ET LIGANDS

DIALOG(R) File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

NUCLEOTIDE AND PROTEIN SEQUENCES OF VERTEBRATE DELTA GENES AND METHODS. BASED THEREON. SEQUENCES. NUCLEOTIDIQUES ET PROTEIQUES DE GENES DELTA DE VERTEBRES ET PROCEDES FONDES SUR CES DERNIERES

14/Ti/4 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. NUCLEOTIDE AND PROTEIN SEQUENCES OF LATS GENES AND METHODS BASED THEREON. SEQUENCES NUCLEOTIDIQUES ET PROTEIQUES DE GENES LATS ET PROCEDES LES. UTILISANT

14/TI/5 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv.
DELTEX PROTEINS, NUCLEIC ACIDS, AND ANTIBODIES, AND RELATED METHODS AND COMPOSITIONS PROTEINES ET ACIDES
DELTEX PROTEINS, NUCLEIC ACIDS, AND ANTIBODIES, CONTRE CEUX-CI, ET PROCEDES ET COMPOSITIONS ASSOCIES

14/TI/6 DIALOG(R)FII6 349:(c) 2004 WIPO/Univentio. All rts. reserv. NOVEL NEUTROPHIL INHIBITORS NOUVEAUX INHIBITEURS DE NEUTROPHILES

ON TRANSDUCIN-LIKE ENHANCER OF SPLIT PROTEIN ET COMPOSITIONS A BASE D'ACTIVATEUR DE TYPE 14/TI/7 DIALOG(R)File 349:(q) 2004 WIPO/Univentic. All rts. reserv. HUMAN HOMOLOGS OF THE TRANSDUCIN-LIKE ENHANCER OF SPLIT GENE AND METHODS BASED THEREON HOMOLOGUES HUMAINS DE L'ACTIVATEUR DU TYPE TRANSDUCINE DE GENES FRACTIONNES ET PROCEDES S'Y RAPPORTANT 1471/8 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.
THERAPEUTIC AND DIAGNOSTIC METHODS AND COMPOSITIONS BASED
AND NUCLEIC ACIDS PROCEDES THERAPEUTIQUES ET DIAGNOSTIQUES
TRANSDUCINE DE PROTEINES FRACTIONNEES ET D'ACIDES NUCLEIQUES 14/TI/9 DIALOG(R)File 349;(e) 2004 WIPO/Univentio. Ali rts. reserv. SEQUENCES CHARACTERISTIC OF HUMAN GENE TRANSCRIPTION PRODUCT SEQUENCES CARACTERISTIQUES DU PRODUIT DE TRANSCRIPTION DES GENES HUMAINS

14/TI/10 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All 1ts. reserv. USE OF THIOL REDOX PROTEINS FOR REDUCING DISULFIDE BONDS UTILISATION DE PROTEINES D'OXYDOREDUCTION A BASE DE THIOL POUR REDUIRE DES LIAISONS BISULFURES

14/TI/11 DIALOG(R) File 349:(c) 2004 WIPO/Univentio. All rts. reserv. BINDING DOMAINS IN NOTCH AND DELTA PROTEINS DOMAINES DE LIAISON DANS DES PROTEINES NOTCH ET DELTA

PREPARATION FOR APPLICATION OF ACTIVE SUBSTANCES IN THE FORM OF MINIMUM-SIZED DROPLETS COMPOSITION D'APPLICATION DE FINES GOUTTELETTES DE SUBSTANCES ACTIVES 14/TI/12 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

14/T/13 DIALOG(R)File 349(c) 2004 WIPO/Univentio. All 1s. reserv. RECOMBINANT CMV NEUTRALIZING PROTEINS PROTEINES RECOMBINANTES DE NEUTRALISATION DE CMV

SOLATION 14/TI/14 DIALOG(R)FIIe 349;(c) 2004 WIPO/Univentio. All rts. reserv. ISOLATION, PURIFICATION, CHARACTERIZATION, CLONING AND SEQUENCING OF N-ALPHA ACETYLTRANSFERASE PURIFICATION, CARACTERISATION, CLONAGE ET MISE EN SEQUENCE DE N-ALPHA ACETYLTRANSFERASE

18/TI/1 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. ADENOVIRAL MEDIATED GENE TRANSFER IN ADIPOCYTES AND RELATED IMPLANTS TRANSFERT DE GENES PAR MEDIATION ADENOVIRALE DANS DES ADIPOCYTES ET IMPLANTS ASSOCIES

18/71/2DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All 1s. reserv. TIE-2 RECEPTOR LIGANDS (TIE LIGAND-3; TIE LIGAND-4) AND THEIR USES. LIGANDS DE RECEPTEURS DE TIE-2 (LIGANDS-3 TIE; LIGANDS-4 TIE) ET LEURS. UTILISATIONS

1871/3 DIALOG(RIFIIe 349;(e) 2004 WIPO/Univentio. All rts. reserv. CYCLIN-C VARIANTS, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF VARIANTES DE CYCLINE-C, LEURS UTILISATIONS DIAGNOSTIQUES ET THERAPEUTIQUES

18/TI/4 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. CYCLIN D BINDING FACTOR, AND USES THEREOF FACTEUR DE LIAISON DE LA CYCLINE DE TYPE D ET EMPLOIS DUDIT PRODUIT

1871/5 DIALOG(R)File 349;(c) 2004 WIPO/Univentio, All rts. reserv.
IDENTIFICATION AND ISOLATION OF NOVEL POLYPEPTIDES HAVING WW DOMAINS AND METHODS OF USING SAME
ET ISOLEMENT DE NOUVEAUX POLYPEPTIDES AYANT DES DOMAINES WW ET PROCEDES D'UTILISATION

18/TI/6 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. Ali rts. resen. GROWTH FACTOR INDUCIBLE SERINE/THREONINE PHOSPHATASE FIN13 SERINE/THREONINE PHOSPHATASE FIN13 MODULANT I FACTEUR DE CROISSANCE

18/TI/7 DIALOG(R)File 349;(c) 2004 WIPO/Univentio, All rts. reserv. MAMMALIAN ENDONUCLEASE III, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF ENDONUCLEASE III DE MAMMIFERES, UTILISATIONS DIAGNOSTIQUES ET THERAPEUTIQUES DE CETTE ENZYME

18/T/8DIALOG(R)File 349; (c) 2004 WIPO/Univentio. All 1ts. reserv. VERTEBRATE DELTEX PROTEINS NUCLEIC ACIDS, AND ANTIBODIES, AND RELATED METHODS AND COMPOSITIONS PROTEINES ACIDES NUCLEIQUES ET ANTICORPS DELTEX DE VERTEBRES, ET PROCEDES ET COMPOSITIONS RELATIFS A CEUX-CI

1871/9 DIALOG(R)File 349;(p) 2004 WIPO/Univentio. All rts. reserv. BIOLOGICALLY ACTIVE EPH FAMILY LIGANDS LIGANDS BIOLOGIQUEMENT ACTIFS DE LA FAMILLE DES EPH

1871/10 DIALOG(R)File 349:(q) 2004 WIPO/Univentio. All rts. reserv. PROTEINS INVOLVED IN TARGETING OF PEPTIDYL TRANSFER CENTER, AND CORRESPONDING THERAPEUTIC AGENTS AND METHODS PROTEINES IMPLIQUEES DANS LE CIBLAGE DU CENTRE DE TRANSFERT DE PEPTIDYLE, ET PROCEDES ET AGENTS THERAPEUTIQUES CORRESPONDANTS

PROCEDES ET VECTEURS PERMETTANT UNE RECOMBINAISON 18/TI/11 DIALOG(R)File 349.(c) 2004 WIPO/Univentio. All rts. reserv. METHODS AND VECTORS FOR SITE-SPECIFIC RECOMBINATION

1871/12 DIALOG(R)File 349;(e) 2004 WIPO/Univentio. All rts. reserv. GENETIC ALTERATIONS RELATED TO FAMILIAL ALZHEIMER'S DISEASE ALTERATIONS GENETIQUES LIEES A LA MALADIE D'ALZHEIMER FAMILIALE

MODULATORS OF EXPRESSION AND FUNCTION OF LRP IN ALZHEIMER'S DISEASE MODULATEURS D'EXPRESSION ET DE FONCTION DE LA PROTEINE ASSOCIEE AU RECEPTEUR DE LA LIPOPROTEINE BASSE DENSITE (LRP) DANS LA MALADIE D'ALZHEIMER 18/TI/13 DIALOG(R) File 349:(c) 2004 WIPO/Univentic. All rts. reserv.

SEQUENCE DE NUCLEOTIDES ET D'ACIDES AMINES ET SES 18/TI/14 DIALOG(R)File 349:(e) 2004 WIPO/Univentio. All rts. reserv. NUCLEOTIDE AND AMINO ACID SEQUENCE AND USES THEREOF UTILISATIONS

METHOD FOR SCREENING FOR RECEPTOR AGONISTS AND ANTAGONISTS PROCEDES DE DEPISTAGE D'AGONISTES 18/TI/15 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. D'ANTAGONISTES DE RECEPTEURS

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RECOMBINANT VESICULOVIRUSES AND THEIR USES VESICULOVIRUS DE RECOMBINAISON ET LEURS UTILISATIONS 18/TI/16 DIALOG(R) File 349:(c) 2004 WIPO/Univentio. All rts. reserv

18/TI/17 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. NUCLEOTIDE SEQUENCE OF THE HAEMOPHILUS INFLUENZAE Rd GENOME, FRAGMENTS THEREOF, AND USES THEREOF SEQUENCE NUCLEOTIDIQUE DU GENOME HAEMOPHILUS INFLUENZAE RD, DES FRAGMENTS DE CE DERNIER, AINSI QUE:

POLYPEPTIDES POLYPEPTIDES HAVING A FUNCTIONAL DOMAIN OF INTEREST AND METHODS OF IDENTIFYING AND USING SAME IPRESENTANT UN DOMAINE FONCTIONNEL IMPORTANT, ET LEURS PROCEDES DIDENTIFICATION ET D'UTILISATION 18/TI/18 DIALOG(R) File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

18/TI/19 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rs. reserv. TIE-2 LIGANDS, METHODS OF MAKING AND USES THEREOF LIGANDS TIE-2, PROCEDES D'OBTENTION DE CES LIGANDS ET LEURS UTILISATIONS

PEPTIDE GROWTH FACTOR HAVING EPIDERMAL INDUCING ACTIVITY FACTEUR DE CROISSANCE PEPTIDIQUE AYANT UNE ACTIVITE INDUISANT L'EPIDERME 18/TI/20 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

18/TI/21 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. resenv. NUCLEOTIDE AND PROTEIN SEQUENCES OF VERTEBRATE SERRATE GENES AND METHODS BASED THEREON SEQUENCES NUCLEOTIDIQUES ET PROTEIQUES DU GENE DENTELE CHEZ LES VERTEBRES ET PROCEDES FONDES SUR CES SEQUENCES

1871/22 DIALOG(R)File 349:(e) 2004 WIPO/Univentio. Ali rts. reserv.

IDENTIFICATION OF DEC, (DENTRITIC AND EPITHELIAL CELLS, 208 KD3), A RECEPTOR WITH C-TYPE LECTIN DOWAINS, NUCLEIC
ACIOS ENCODING DEC, AND USES THEREOF IDENTIFICATION DE LA PROTEINE MEMBRANAIRE, INTEGRALE DEC (CELLULES
DENDRITIOLES ET EPITHELIALES, 205 KD3), UN RECEPTEUR A DOMAINES LECTINIQUES DE TYPE C, DES ACIDES NUCLEIQUES
CODANT DEC, AINSI QUE SES APPLICATIONS

18/TI/23DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. PEPTIDES SPECIFIC FOR THE FIRST Crk-SH3 DOMAIN PEPTIDES SPECIFIQUES DU PREMIER DOMAINE SH-3 DE Crk

DOMAINES 18/TI/24 DIALOG(R) File 349;(c) 2004 WIPO/Univentio. All rts. reserv. FUNCTIONALLY ACTIVE DOMAINS OF SIGNAL TRANSDUCER AND ACTIVATORS OF TRANSCRIPTION (STAT) PROTEINS DOM. FONCTIONNELLEMENT ACTIFS DE PROTEINES TRANSDUCTEURS DE SIGNAUX ET ACTIVATEURS DE TRANSCRIPTION (STAT)

18/TI/25 DIALOG(R)File 349.(c) 2004 WIPO/Univentio. All rs. reserv.
METHODS AND COMPOSITIONS FOR INHIBITION OF MEMBRANE FUSION-ASSOCIATED EVENTS, INCLUDING HIV TRANSMISSION
PROCEDES ET COMPOSITIONS POUR EMPECHER CERTAINS PHENOMENES ASSOCIES AVEC LA FUSION AVEC LA MEMBRANE,
PARTICULIER LA TRANSMISSION DU VIH

18/TI/26 DIALOG(R)File 349(c) 2004 WIPO/Univentio. All 16. reserv. AN SH3 KINASE DOMAIN ASSOCIATED PROTEIN, A SIGNALLING DOMAIN THEREIN, NUCLEIC ACIDS ENCODING THE PROTEIN AND THE DOMAIN, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF PROTEINE ASSOCIEE AU DOMAINE SH3 DE LA KINASE,

DOMAINE DE SIGNALISATION DANS CETTE PROTEINE, ACIDES NUCLEIQUES CODANT CETTE PROTEINE ET UTILISATIONS DIAGNOSTIQUES ET THERAPEUTIQUES DE CETTE PROTEINE

CES NEUTRALIZATION OF FOOF ALLERGENS BY THIOREDOXIN NEUTRALISATION D'ALLERGENES ALIMENTAIRES PAR LA THIOREDOX 18/TI/28DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. TIE-2 LIGANDS, METHODS OF MAKING AND USES THEREOF LIGANDS TIE-2, PEOCEDES DE PRODUCTION ET UTILISATIONS DE 18/TI/27DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv

LIGANDS

18/TI/29 DIALOG(R)File 349.(c) 2004 WIPO/Univentio. All rts. reserv. DENERVATED MUSCLE KINASE (DMK), A RECEPTOR OF THE TYROSINE KINASE SUPER FAMILY KINASE DE MUSCLE ENERVE (DM UN RECEPTEUR DE LA SUPER FAMILLE DES TYROSINES KINASES

COMPOSITIONS COMPRISING COMPLEMENT RELATED PROTEINS AND CARBOHYDRATES, AND METHODS FOR PRODUCING AND USING SAID COMPOSITIONS COMPOSITIONS COMPRENANT DES PROTEINES ET DES GLUCIDES APPARENTES COMPOSITIONS AND COMPUEMENTAIRES, ET LEURS PROCEDES DE PRODUCTION ET UTILISATION DE CES COMPOSITIONS 18/TI/30DI/ALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. MARKERS OF ORGAN REJECTION MARQUEURS DE REJET D'ORGANES 18/T1/31 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

CLONING AND RECOMBINANT PRODUCTION OF VESPID VENOM ENZYMES. SUCH AS PHOSPHOLIPASE AND HYALURONIDASE, AN IMMUNOLOGICAL THERAPIES BASED THEREON. PRODUCTION PAR CLONAGE ET RECOMBINAISON D'ENZYMES DE VENIN DE VESPIDES TELLES QUE LA PHOSPHOLIPASE ET L'HYALURONIDASE, ET THERAPIES. IMMUNOLOGIQUES SY RAPPORTANT 18/TI/32 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv.

18/TI/33 DIALOG(RJFIIe 349:(e) 2004 WIPO/Univentio. All rts. reserv. HUMAN HOMOLOG OF THE E-CADHERIN GENE AND METHODS BASED THEREON HOMOLOGUE HUMAIN DU GENE DE LA CADHER E ET PROCEDES D'UTILISATION

PROCEDES THERAPEUTIC AND DIAGNOSTIC METHODS AND COMPOSITIONS BASED ON NOTCH PROTEINS AND NUCLEIC ACIDS THERAPEUTIQUES ET DIAGNOSTIQUES ET COMPOSITIONS A BASE DE PROTEINES NOTCH ET D'ACIDES NUCLEIQUES 18/Tt/34 DIALOG(R) File 349:(c) 2004 WIPO/Univentio, All rts. reserv

PAPILLOMAVIRUS VACCINÈS VACCIN CONTRE LE PAPILLOMAVIRUS 18/TI/35DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv

187II/36 DIALOG(R)File 349(c) 2004 WIPO/Univentio. All rts. reserv. A NOVEL RECEPTOR FOR alpha4 INTEGRINS AND METHODS BASED THEREON NOUVEAU RECEPTEUR D'INTEGRINES alpha4 ET PROCEDES BASES SUR CELUI∙CI

BINDING PEPTIDES WHICH MTERACT WITH LIGAND GROWTH FACTORS OF THE EPIDERMAL GROWTH FACTOR RECEPTOR AND emb-2-RECEPTOR PEPTIDES FIXATEURS QUI AGISSENT RECIPROQUEMENT AVEC LES FACTEURS DE CROISSANCE DE LIGANDS DU RECEPTEUR DU FACTEUR DE CROISSANCE DE L'EPIDERME ET DU RECEPTEUR DE emb-2 18/TI/37 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv.

SEQUENCES 1871/38 DIALOG(R)FIIe 349.(e) 2004 WIPO/Univentio. All rts. reserv. NUCLEOTIDE AND PROTEIN SEQUENCES OF THE SERRATE GENE AND METHODS BASED THEREON NUCLEOTIDIQUES ET PEPTIDIQUES DU GENE DENTELE ET PROCEDES BASES SUR CES SEQUENCES

HUMAN TUMOR SF-25 ANTIGEN, METHODS 1871/39 DIALOG(R)FIIe 349:(q) 2004 WIPO/Univentio. All ris. resenv. SF-25 ANTIGEN, WETHODS SF-25 ANTIGEN, METHODS SF-25 ANTIGEN, METHODS F-25 ANTIGEN, METHODS FOR THEIR PRODUCTION, AND USES THEREOF ANTICORPS SF-25, NOTAMMENT ANTICORPS CHIMERIQUES SPECIFIQUES DE L'ANTIGENE DE SF-25 DE TUMEURS HUMAINES, LEURS PROCEDES DE PREPARATION ET LEUR UTILISATION 18/71/40 DIALOG(R) File 349;(e) 2004 WIPO/Univertio. All rts. reserv. LIGAND GROWTH FACTORS THAT BIND TO THE erbB-2 RECEPTOR PROTEIN AND INDUCE CELLULAR RESPONSESFACTEURS DE CROISSANCE LIGANDS QUI SE LIENT AU RECEPTEUR PROTEIQUE erbB-2 ET INDUISENT DES REPONSES CELLULAIRES

TUMOR SUSCEPTIBLE NON-HUMAN ANIMALS ANIMAUX NON HUMAINS SUSCEPTIBLES D'AVOIR UNE TUMEUR 18/TI/41 DIALOG(R) File 349:(c) 2004 WIPO/Univentio. All rts. reserv

CONJUGUES DE PROTEINS POLY(VINYLSACCHARIDE) AVEC DES PROTÉINES POUR LA STABILISATION DE PROTEINES 18/Ti/42 DIALOG(R)File 349.(c) 2004 WIPO/Univentio. All rts. reserv. CONJUGATES OF POLY(VINYLSACCHARIDE) WITH PROTEINS FOR THE STABILIZATION OF

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18/TI/43 DIALOG(R)File 349;(e) 2004 WIPO/Univentio. All rts. resenv. GLYCOPROTEIN HORMONE RECEPTOR MOLECULES MOLECULES RECEPTRICES D'HORMONE DE GLYCOPROTEINE

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DETERMINATION OF FACTORS AFFECTING GENE REGULATION AND/OR GENE REPLICATION DETERMINATION DES FACTEURS AFFECTANT LA REGULATION ET/OU LA REPLICATION DE GENES

18/TI/45 DIALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. HUMAN HEAT SHOCK FACTOR FACTEUR DE CHOC THERMIQUE HUMAIN 1877/46 DIALOG(R)FIIe 349;(c) 2004 WIPO/Univertio, Ali 1s. reserv. SF-25 COLON ADENOCARCINOMA ANTIGEN, AND ANTIBODIES WHICH RECOGNIZE THIS ANTIGEN ANTIGENE SF-25 DE L'ADENOCARCINOME DU COLON ET ANTICORPS RECONNAISSANT CET ANTIGENE 18TI/47 DIALOG(R)File 349:(c) 2004 WIPO/Univentio. All rts. reserv. CARCINOMA-ASSOCIATED ANTIGENS, AND ANTIBODIES WHICH RECOGNIZE THESE ANTIGENS, ANTIGENES ASSOCIES AU CARCINOME ET ANTICORPS LES RECONNAISSANT

21/TI/10IALOG(R)File 349;(c) 2004 WIPO/Univentio. All rts. reserv. RTK/CYTOKINE RECEPTOR CHIMERAS RECEPTEURS CHIMERES DE RTK/CYTOKINE

21/TI/2 DIALOG(R)File 349:(q) 2004 WIPO/Univentio. All rts. reserv. APTAMER SPECIFIC FOR BIOMOLECULES AND METHOD OF MAKING APTAMERE SPECIFIQUE DE BIOMOLECULES ET PROCEDE DE PRODUCTION